PA JT COOPERATION TREAT

From the INTERNATIONAL BUREAU

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NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day month year) 14 June 2000 (14.06.00)	
International application No. PCT/EP99/08306	**Applicant's or agent's file reference** FC 857 5
International filing date (day month year) 27 October 1999 (27.10.99)	**Priority date** (day month year) 30 October 1998 (30.10.98)
Applicant PEVARELLO, Paolo et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

15 May 2000 (15.05.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Claudio Borton

Telephone No.: (41-22) 338.83.38

'PATENT COOPERATION TREATY

USA

From the INTERNATIONAL BUREAU

HP

PCT

To:
PHARMACIA & UPJOHN S.P.A.
Patent Department
Viale Pasteur, 10
I-20014 Nerviano
ITALIE

NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

Date of mailing (day/month/year) 11 May 2000 (11.05.00)	
Applicant's or agent's file reference FC 857/5	**IMPORTANT NOTICE**

International application No.	**International filing date** (day/month/year)	**Priority date** (day/month/year)
PCT/EP99/08306	27 October 1999 (27.10.99)	30 October 1998 (30.10.98)

Applicant
PHARMACIA & UPJOHN S.P.A. et al

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:
   AU,CN,JP,KP,KR,US

   In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:
   AL,AP,BA,BB,BG,BR,CA,CU,CZ,EA,EE,EP,GD,GE,HR,HU,ID,IL,IN,IS,LC,LK,LR,LT,LV,MG,MK,
   MN,MX,NO,NZ,OA,PL,RO,SG,SI,SK,SL,TR,TT,UA,UZ,VN,YU,ZA

   The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on
   11 May 2000 (11.05.00) under No. WO 00/26202

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, **a demand for international preliminary examination** must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the **national phase**, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer J. Zahra
Facsimile No. (41-22) 740.14.35	Telephone No. (41-22) 338.83.38

Form PCT/IB/308 (July 1996)

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PATENT COOPERATION TREATY

REC'D 17 JAN 2001

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
FC 857/5		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP99/08306	27/10/1999	30/10/1998
International Patent Classification (IPC) or national classification and IPC C07D277/46		
Applicant PHARMACIA & UPJOHN S.P.A. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 13 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☒ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
15/05/2000	15.01.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Cortés, J Telephone No. +49 89 2399 8206

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP99/08306

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:
Description, pages:

1-81 as originally filed

Claims, No.:

1-14 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	3, 5, 11
	No:	Claims	1-2, 4, 6-10, 12-14
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-14
Industrial applicability (IA)	Yes:	Claims	1-14
	No:	Claims	

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: WO 98 04536 A (OTSUKA PHARMACEUTICAL COMPANY LIMITED) 5 February 1998 (1998-02-05) cited in the application

D2: EP-A-0 412 404 (FUJISAWA PHARMACEUTICAL CO) 13 February 1991 (1991-02-13) cited in the application

D3: US-A-4 027 031 (DEBAUN JACK R ET AL) 31 May 1977 (1977-05-31)

D4: DE 21 28 941 A (SOCIETE MELLE-BEZONS) 16 December 1971 (1971-12-16) cited in the application

D5: EP-A-0 261 503 (VALEAS SPA) 30 March 1988 (1988-03-30) cited in the application

D6: CHEMICAL ABSTRACTS, vol. 50, no. 1, 10 January 1956 (1956-01-10) Columbus, Ohio, US; abstract no. 964e, S.R.M.BUSHBY ET AL: 'The antitrichomonal activity of amidonitrothiazoles' page 964; XP002130674 & J.PHARM. AND PHARMACOL., vol. 7, 1955, pages 112-117

D7: CHEMICAL ABSTRACTS, vol. 61, no. 3, 3 August 1964 (1964-08-03) Columbus, Ohio, US; abstract no. 3087, MAX ROBBA ET AL: 'Synthesis of thiazoles and isothiazoles.Their action on Trichomonas vaginalis and Candida albicans' XP002130675 & ANN. PHARM. FRANC., vol. 22, no. 3, 1964, pages 201-210

D8: PETER J. ISLIP ET AL: 'Schistosomicidal 5-nitro-4-thiazolines' JOURNAL OF MEDICINAL CHEMISTRY., vol. 15, no. 9, 1972, pages 951-954, XP002130668 AMERICAN CHEMICAL SOCIETY. WASHINGTON., US ISSN: 0022-2623

D9: ROGER D. WESTLAND ET AL: 'Novel schistomicides. S-2-[2-2(2-thiazolylcarbamoyl)ethyl]amino ethyl hydrogen thiosulfate and related compounds' JOURNAL OF MEDICINAL CHEMISTRY., vol. 14, no. 10, 1971, pages 916-920, XP002130669 AMERICAN CHEMICAL SOCIETY. WASHINGTON., US ISSN: 0022-2623

D10: LEIF GREHN: 'A method for nitration of thiazoles' JOURNAL OF HETEROCYCLIC CHEMISTRY., vol. 14, no. 5, August 1977 (1977-08), pages 917-919, XP002130670 HETEROCORPORATION. PROVO., US ISSN: 0022-152X

D11: US-A-3 427 318 (BARBER MICHAEL STUART ET AL) 11 February 1969 (1969-02-11)

D12: H.ERLENMEYER ET AL: 'Zur Kenntnis der Thiazol-4-sulfonsäure und der Thiazol-5-sulfonsäure' HELVETICA CHIMICA ACTA., vol. 28, 1945, pages 985-991, XP002130671 VERLAG HELVETICA CHIMICA ACTA. BASEL., CH ISSN: 0018-019X

D13: FR-A-1 499 557 (MAY AND BAKER LIMITED) 18 September 1967 (1967-09-18)

D14: US-A-3 591 600 (FANCHER LLEWELLYN W) 6 July 1971 (1971-07-06)

D15: FR-A-1 488 625 (TOYO KOATSU INDUSTRIES INC.) 5 June 1967 (1967-06-05)

D16: DE 16 42 352 A (MITSUI TOATSU CHEMICALS) 24 February 1972 (1972-02-24)

D17: CHARLES D. HURD ET AL: 'The 2-aminothiazoles' JOURNAL OF THE AMERICAN CHEMICAL SOCIETY., vol. 71, December 1949 (1949-12), pages 4007-4010, XP002130672 AMERICAN CHEMICAL SOCIETY, WASHINGTON, DC., US ISSN: 0002-7863

D18: TIMOTHY N. BIRKINSHAW ET AL: 'Tautomerism in 2-trichloro- and 2-trifluoro-acetamidothiazoles' JOURNAL OF THE CHEMICAL SOCIETY, PERKIN TRANSACTIONS 1.,1982, pages 939-943, XP002130673 CHEMICAL SOCIETY. LETCHWORTH., GB ISSN: 0300-922X

D19: US-A-3 374 082 (LEMIN ALAN J) 19 March 1968 (1968-03-19)

D20: CHEMICAL ABSTRACTS, vol. 81, no. 5, 5 August 1974 (1974-08-05) Columbus, Ohio, US; abstract no. 22258q, page 156; XP002130676 & JP 48 027467 B (SANKYO CO LTD) 22 August 1973 (1973-08-22) cited in the application

D21: WO 99 65884 A (BRISTOL-MYERS SQUIBB COMPANY) 23 December 1999 (1999-12-23)

Novelty

There is a substantial overlap between the subject matter of present claims 1, 2, 4, 6-10 and 14 and the subject-matter disclosed in D1 (D1: e.g. claims 1, 2, 3, 4, 5, 18, 19, 20, 21, 26, 27 and 31, pages 410-422). All structural features of present compounds are covered by examples in D1 (D1: e.g. examples 105, 106, 217, 235-237, 250, 312, pages 152, 153, 293, 300-301, 305, 328).

A kinase inhibitory activity as well as a potential activity in the regulation of cell proliferative disorders and consequently a possible use as pharmaceutical active drug substance are also described in D1 (D1: e.g. p. 6, line 18 to page 7, line 18).

The following diseases are disclosed in D1: e.g. cancer, Alzheimer's disease, HIV infection, autoimmune diseases such as psoriasis and arteriosclerosis (D1: e.g. page 7).

D1 also discloses the preparation of several pharmaceutical formulations (D1: e.g. page 101-108).

Therefore, the subject matter of claims 1, 2, 4, 6-10 and 14 is not novel in view of D1.

The following compounds described in D2 are encompassed by claim 1: 2-acetylamino-5-chlorothiazole (D2: examples 16, 22, 28, 32, 39, 55, 57, 61 on pages 19-21, 23, 24, 28, 29, 30) and 2-acetylamino-5-bromothiazol (D2: examples 67, 69, 72, 76, 79, 82 on pages 31, 32, 33, 34, 35, 36).

These compounds were used in D2 as starting materials in the synthesis of pharmaceutically active compounds for the treatment of e.g. rheumatism, nephritis or tumor (D1: page 3; claims 8-13 on pages 41-43), i.e. they were used "... in the manufacture of a medicament for treating ..." the mentioned diseases, as stated in claims 1 and 2.

An acylation according to present claims 12 and 13 is also described in D2 (D2: e.g. process 7 on page 5).

Accordingly, the subject-matter of claims 1, 2, 6-10, 12-14 is not novel in view of D2.

D3 discloses two compounds according of formula (I) in which R_1 is cyclopropyl and R is a chloro or bromo, as well as their use in pharmaceutical compositions and their synthesis by acylation of the 2-aminothiazols (D3: compounds no. 1 and 2, column 1, lines 25-45). Consequently D3 describes part of the subject matter of claims 6, 7, 12-13 and 14.

D4 discloses compounds according to formula (I) in which R_1 is a substituted aminomethyl-group such as (1-piperidyl)methyl, (4-morpholinyl)methyl, (2-furfuryl)aminomethyl, (4-(2-hydroxyethyl)-1-piperazinyl))methyl, (4-morpholinyl)ethylaminomethyl and R is a chloride (D4: e.g. page 2, 3; examples 2-5, 7, pages 6-9, 14), as well as an acylation according to present claims 12-13 (D4: page 4) and their use in pharmaceutical compositions. Therefore claims 6, 12-13 and 14 are not novel in view of D4.

D7 describes the synthesis of the following compounds according to formula (I): e.g. 2-[SPEC0803]-thienyl-oxoimino-5-nitro-1,3-thiazole (R_1= [SPEC0803]-thienyl, R= nitro), 2-α-furyl-oxoimino-5- chloro-1,3-thiazole (R_1= α-furyl, R= chloro), 2-α-thienyl-oxoimino-5-chloro-1,3-thiazole (R_1= α-thienyl, R= chloro), 2-[SPEC0803]-thienyl-oxoimino-5-chloro-1,3-thiazole (R_1=[SPEC0803]-thienyl, R= chloro), 2-α-furyl-oxoimino-5-bromo-1,3-thiazole (R_1= α-furyl, R= chloro), 2-α-thienyl- oxoimino-5-bromo-1,3-thiazole (R_1= α-thienyl, R= bromo), 2-[SPEC0803]-thienyl-oxoimino-5- bromo-1,3-thiazole (R_1=[SPEC0803]-thienyl, R= bromo) as well as their preparation from the respective 2-amino-1,3-thiazole derivatives by acylation. Thus D7 discloses subject matter encompassed by claims 6, 7, 12-13.

D8 discloses compounds according to formula (I) with R= NO_2 and R_1= Me, Et, tert.-Bu, i-Pr, Ph, CCl_3 (D8: reaction scheme on page 951 and starting compounds for the manufacture of compounds 1-45 in table I on page 952), which are within the scope of claims 6, 7 and 10.

D9 describes the synthesis of 3-[(2-Chloroethyl)amino]-N-(5-nitro-2-thiazolyl)propionamide hemisulphate (R= NO_2, R_1= $(CH_2)_2NH(CH_2)_2Cl$) (D9: e.g. compound 12 on pages 917 and 920), which are encompassed by claims 6, 7 and 10.

D10 discloses compounds according to formula (I) with the following substituents: R_1= CH_3, R= i-Pr, tert.-Bu, Cl (D10: e.g. reaction scheme on page 917, compounds I a-c). Accordingly claims 7-10 are not novel.

D11 discloses compounds according to formula (I) such as e.g. 5-iodo-2-propionamidothiazole (R= I, R_1= Et) (D11: example I in column 4, line 35; example VII in column 8, line 23; example XVI in column 9, line 27), 5-chloro-2-hexanamidothiazole (R= Cl, R_1= pentyl) (D11: example XIV in column 9, line 4), 5-chloro-2-(2-methylvaleramido)thiazol (R= Cl, R_1= 1-methyl-butyl) (D11: example XV in column 9, line 10), 2-isobutyramido-5-iodothiazol (R= I, R_1= i-Pr) (D11: example XII in column 9, line 44), as well their synthesis by acylation of the amino compounds (D11: column 5, lines 60-70). Therefore the subject matter of claims 7-10 and 12-13 is not novel.

D13 discloses three compounds according to formula (I) wherein R_1 is cyclopropyl and R is chlorine, bromine and iodine (D13: compounds A-C on page 4) as well as their synthesis according to present claims 12-13 (D13: e.g. synthesis B on page 6). Hence claims 7-9 and 12-13 are not novel.

In the compounds described in D14 R is a substituted phenyl, a nitro or bromo group and R_1= $CH_2SP(S)R_3R_4$ wherin R_3 and R_4 are independently ethoxy, ethyl or methoxy (D14: e.g. compounds 32, 38, 39, 41, 42 and 44 in table I columns 3-6). Consequently claims 7-10 are not novel.

D15 and D16 disclose both the exemplary compound 2-acryloylamino-5-bromo-1,3-thiazole (D15: in table 1 on page 2; D16: in table I, page 6) in which R_1 is ethenyl and R is bromine. This compound is comprised in claims 7-9.

D18 discloses compounds containing the following substituents: R_1= CH_2Cl, $CHCl_2$, CCl_3, CF_3; R= Et, $PhCH_2$ (D18: e.g. exemplary compounds 1a and 1b with R_3=CH_2Cl, CHCl, $CHCl_2$, CCl_3, CF_3 on page 939 and tables 1 and 2 on pages 941 and 943). As well as the acylation of the 2-amino-1,3-thiazoles (D18: e.g. reaction scheme on page 939). Therefore claims 7-10 and 12-13 are not novel.

Consequenly, the subject matter of claims 1-2, 4, 6-10 and 12-14 is not novel and does not fulfill the requirements of Art. 33(2) PCT.

The subject matter of present claims 1, 2, 6-10 and 12-14 overlaps with the subject matter disclosed in D5 (D5: e.g. claims 1, 2 and 14, pages 27-30).

D5 generically discloses compounds according to formula (I) (D5: e.g. claim1, page 27-28), an acylation according to present claims 12-13 (D5: e.g. claim 2, p. 28-29) as well as their use as pharmaceutical active substances or as starting compounds for the synthesis of pharmaceutical active substances as well as the preparation of pharmaceutical compositions containing these compounds for the treatment of allergic affections (D5: e.g. claim 14, page 30 and description, page 26).

Nonetheless, present compounds differ from the exemplary 2-amino-1,3-thiazoles disclosed in D5 in the group R and the unsubstituted 4-position.

Present compounds differ from the compound disclosed in D6 in the group R_1.

D12 discloses a disclaimed compound (R_1= CH_3, R= Br; D2: e.g. 2-acetyl-amino-5-bromo-1,3-thiazol, page 989).

D17 discloses the synthesis of several disclaimed compounds, such as: e.g. 5-phenyl-2-acetamido-1,3-thiazole, 5-nitro-2-acetamido-1,3-thiazol, 5-bromo-2-acetamido-1,3-thiazole, 5-iodo-2-acetamido-1,3-thiazole (R= Ph, NO_2, Br, I; R_1= CH_3; D17: e.g. page 4009).

D19 and D20 disclose disclaimed compounds (D19: R_1= Me, Et and R= Br, Cl, I; e.g. examples 1-4, columns 5-6; D20: R_1= Et, i-Pr and R= Cl, Br).

Inventive Step

D1 describes a group of compounds according to formula (I) with the following structural features (D1: see e.g. claim 1 on page 410: definition of R^1=H, u=0, R^4=H): R_1= a substituted C_1-C_6 alkyl or a substituted pyperidine (D1: see definition of R^3); R= C_1-C_6 alkyl (D1: see definition of R^2= lower alkyl and definition of lower alkyl on page 7).

A kinase inhibitory activity as well as a potential activity in the regulation of cell proliferative disorders and consequently a possible use as pharmaceutical active drug substance are also described in D1 (D1: e.g. line 18, page 6 to line 18, page 7), as well as a potential use for the treatment of the following diseases: e.g. cancer, Alzheimer's disease, HIV infection and autoimmune diseases (D1: page 7).

D1 also discloses the preparation of several pharmaceutical formulations (D1: e.g. page 101-108).

D2 discloses the following structural features (D2: see e.g. claim 1 on page 37): Basic structure containing a 1,3 thiazol with an oxoaminogroup in 2-position, wherein R_1 can be different specific alykl, alkenyl, aryl and many other groups (D1: see definition of R^1= acyl and definition of acyl on page 7, lines 10-24; R^2=H); R= a substituted arylmethylene group (D1: see definition of A= -CH_2- and R^3= aryl).

As already explained under "novelty", D2 also discloses two compounds that are within the scope of present application as well as their preparation and some of the claimed medical indications.

D5 discloses compounds according to formula (I) in which R_1 is a substituted aryl and R is a linear C_1-C_4 alkyl (D5: claim 1, page 27-28), as well as an acylation according to claims 12-13 (D5: claim 2, page 28-29) and their use as pharmaceutical active substances or as starting compounds for the synthesis of pharmaceutical active substances as well as the preparation of pharmaceutical compositions containing these compounds for the treatment of allergic affections (D5: description, page 26 and claim 14, page 30).

Present subject matter differs from the exemplary compounds described in D1 and D5.

The group of compounds claimed in present application strongly overlaps with the groups of compounds described in D1, D2 and D5 for the same medical indications.

The problem of finding alternative active substances for the treatment of the diseases listed in claims 2-5 to the compounds already known from D1, D2 and D5 was solved by selecting sub-sets of the groups of compounds already disclosed in D1, D2 and D5 or by replacing substituents by equivalent groups, circumventing already known specific compounds.

Since this is an obvious measure of providing alternatives with similar properties, present subject matter does not fulfill the requirements for inventiveness according to Article 33(3) PCT.

An inventive step could be acknowledged, if it were shown that novel compounds have unexpected properties or advantages when compared to the stucturally closest related compounds described in D1, D2 and D5.

It is pointed out in this context that the properties establishing an inventive step should extend to the whole of the scope claimed. In view of the close state of the art, it appears that only specific compounds with proved unexpected properties could be claimed, since it would not be possible to generalise a specific compound fulfilling this requirement.

Up to now, no specific results showing any effect for any compound have been presented. It is only stated generally that "The compounds of formula (I) ... gave positive results" in the cdk/cyclin inhibitor test. There is no information about which compounds were tested or which results were found when compared to which known substances.

Re Item VI
Certain documents cited

The priority documents pertaining to the present application were not available at the time of establishing this report. Hence, it is based on the assumption that all claims enjoy priority rights from the filing date of the priority document. If it later turns out that this is not correct, the document D21 cited in the international search report could become relevant to asses whether the present claims satisfy the criteria set forth in Article 33(1) PCT.

Re Item VII
Certain defects in the international application

To meet the requirements of Rule 5.1(a)(ii) the above mentioned prior art should be cited in the description.

Re Item VIII

Certain observations on the international application

Claim 11 is not clear and concise. In deciding this matter, the interest of the relevant public had to be take into account, since patents should not be allowed to erect a legal maze or smoke screen in front of potential users of claimed inventions.

Patent claims, taken singly as well as in totality, must be clear and concise in order to enable potential users to ascertain, without undue burden, let alone recourse to litigation, whether their planned commercial use is likely to infringe the patent.

Having to construe the formulae of hundreds of compounds in order to form a valid and commercially useful opinion on whether or not any one of them could prevent or hinder the commercial activities, must in the nature of things impose a severe and totally undue burden on the public.

It follows that said claim falls foul of the clear provision not only of Rule 13(4) but also of Article 6 PCT.

ENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
FC 857/5		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/EP 99/ 08306	27/10/1999	30/10/1998
Applicant		
PHARMACIA & UPJOHN S.P.A. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

[ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readble form.

[ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

[X] the text is approved as submitted by the applicant.

[ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

[X] the text is approved as submitted by the applicant.

[ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. –

[ ] as suggested by the applicant.

[ ] because the applicant failed to suggest a figure.

[ ] because this figure better characterizes the invention.

[ ] None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
[redacted]EP 99/08306

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D277/46 C07D417/12 A61K31/426 A61K31/427 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 04536 A (OTSUKA PHARMACEUTICAL COMPANY LIMITED) 5 February 1998 (1998-02-05) cited in the application page 101, line 22 -page 108, line 9; claims	1-14
X	EP 0 412 404 A (FUJISAWA PHARMACEUTICAL CO) 13 February 1991 (1991-02-13) cited in the application claims	1-14
X	US 4 027 031 A (DEBAUN JACK R ET AL) 31 May 1977 (1977-05-31) the whole document	1-14

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
16 February 2000	02/03/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Henry, J

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Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
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X	CHEMICAL ABSTRACTS, vol. 50, no. 1, 10 January 1956 (1956-01-10) Columbus, Ohio, US; abstract no. 964e, S.R.M.BUSHBY ET AL: "The antitrichomonal activity of amidonitrothiazoles" page 964; XP002130674 abstract & J.PHARM. AND PHARMACOL., vol. 7, 1955, pages 112-117,	1-14
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X	PETER J. ISLIP ET AL: "Schistosomicidal 5-nitro-4-thiazolines" JOURNAL OF MEDICINAL CHEMISTRY., vol. 15, no. 9, 1972, pages 951-954, XP002130668 AMERICAN CHEMICAL SOCIETY. WASHINGTON., US ISSN: 0022-2623 the whole document	1-14
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International Application No
P[redacted]EP 99/08306

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	FR 1 488 625 A (TOYO KOATSU INDUSTRIES INC.) 5 June 1967 (1967-06-05) claims	6-13
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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E	WO 99 65884 A (BRISTOL- MYERS SQUIBB COMPANY) 23 December 1999 (1999-12-23) claims -----	1-14

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